ESMO Clinical Unit Visit Report

Kantonsspital Sankt Gallen
Sankt Gallen, Switzerland

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Clinical research unit visit at Department of Haematology and Oncology

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Mentor(s): Markus Joerger
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I am a resident of medical oncology in my last year of training. During my years of training I have gotten really interested in a drug development, early and later phases of clinical trials. I contacted dr Markus Joerger, a Phase I researcher at Kantonsspital St. Gallen (KSSG), which accepted me for a Clinical Unit visit under his mentorship. My aim was to get in touch with Phase I studies which at the present moment are not conducted at my home institution and there is a potential aim to implement early phase clinical trials in our clinical research work. An additional aim was getting in touch with a different health and hospital system.

During my stay at KSSG I was mainly participating at daily activities of dr Joerger with addition to follow the weekly plan we have proposed to ESMO. The main goal of my visit at KSSG was to build up expertise in conducting phase I clinical studies. With dr. Joerger, we have made a systematic overview on planning, preparing and executing Phase I trials. This included specific learning (on real-life examples) how to review trial proposals from potential Industry sponsors, protocol writing, documentation within interventional trials, SAE management, monitoring and regular safety calls within early-stage clinical trials. With examples of different Phase I clinical trials, we discussed advantages and disadvantages of different methodological approaches: more common 3+3 design or newer model based approaches.

An important part of study preparation is writing a study protocol. We have looked to a few different Phase I and also Phase II or III study protocols; what is a general structure of a study protocol and also differences in industry-initiated study protocols or investigator-initiated (IIT) study protocols. A specific point during protocol preparation is communicating with sponsors or academic groups which are initiating the trial. I have participated in communication of study protocol preparation or presentation and attracting potential sponsors. In addition, I have also participated in communication with academic organisation (e.g. SAKK) when study protocols have been discussed.

When the study design is agreed and a protocol is approved, the study must also go through the regular approval process. Different authorities are involved in this process: national drug agency, ethics committee additional to the approving process of sponsor/academic group and Clinical Research

Organisation (CRO). When the study is approved on all levels required, the initiation process can be executed. During my stay I have participated at several study initiations (phase I and others).

A critical part of the execution of phase I clinical trials is the organisation and structure of the specific research facilities. Kantonsspital St. Gallen has a special organisation in order to conduct phase I clinical trials, including separate drug storage, preparation and outpatient application rooms. I have also spent few days with Clinical research coordinators (CRC) in order to see their part in phase I trials and especially getting to know how data are collected in the trials and preparing Case Report Forms (CRF). During my stay, there were different phase I trials ongoing which included also different modes of drug application: oral, intravenous and pumps, including more conventional chemotherapeutic drugs as well as immunotherapies and combinations of thereof.

Since the majority of clinical studies ongoing at KSSG were not Phase I, I have gotten a good insight also in these studies: study initiation, study monitoring, patient inclusion. During my stay there were more than 50 studies ongoing in different phases. There were regular monthly meetings of all oncological clinical researchers where ongoing studies have been discussed (stats, number of included patients, issues, etc...) as well as upcoming clinical studies. Each potential study has been discussed from the perspective of feasibility at KSSG: organisational, technical feasibility and availability of patients eligible for study inclusion regarded to the already ongoing studies

At KSSG, there is also a pre-clinical research unit which I have visited several times with dr Joerger during my stay. At meetings, we have discussed about translation of preclinical data into early clinical trials. Usually at such meetings, we discussed data obtained from animal models (pharmacokinetic and pharmacodynamics, toxicity, NOAEL...) and translate them for setting the initial dose in phase clinical trial. Several different agents have been discussed during such meetings for eventual Phase I clinical trial where majority of them were potential candidates for Investigator Inititation trials.

A major part of dr Joerger's daily activities was at the outpatient clinic. I have been seeing with him thoracic cancer patient as well as patients with different advanced solid tumors receiving mainly treatment within clinical studies. A part of an outpatient clinic routine are also weekly meetings of different medical oncologists team regarding to the tumor localisation: gastrointestinal, thoracic and genitourinary. At such meeting oncological patients which are being treated systemically. Besides outpatient clinic I have also seen different oncological inpatient clinic, which are mainly divided to part of haematological oncology, solid tumors and palliative care. I regularly attended different multidisciplinary tumor boards. In KSSG there is a separate unit for breast cancer at which I shortly attended. It is designed to include surgeons, radiotherapists and medical oncologist in one unit.

Education is a part of daily process to which I have attended. Mainly, morning meetings finish with a short internal lecture so called "short cut" where practice changing articles are presented by the relevant medical oncologist. During my stay there was so called onco-lunch where best of ESMO have been presented. I additionaly participated at an internal course on statistics for clinical researchers and one lecture on imunotheraphy combination treatments, which was held in Chur hospital by dr Joerger.

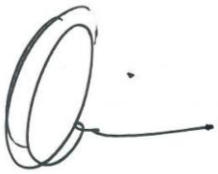
A special, non-formal part of my education in Switzerland was getting in touch with their health care system. Even though a basic organisational structure of Swiss and Slovenian healthcare system may share

some similarities but with a 4 times difference in GDP per capita this results in inevitable differences in patient care. Even though that Slovenia still manages to provide newer oncological drugs by health insurance, the differences between the two countries are mainly shown in availability of diagnostic and therapeutic procedures and amount of time which can be dedicated to a patient from a doctor.

In present, we are witnessing a high rise of newcomming drugs in oncology which also substantially rise a cost of treatment per patient. Clinical studies are more and more important as a tool to offer patients new and expensive drugs. This is especially important for a healthcare systems which struggles with the high costs of a new anticancer drugs. Therefore, I believe, it is crucial for a young oncologist to be trained how to run clinical studies. During my stay at KSSG, I have gotten a good insight how a well organized clinical trial unit should look like and I have learned basic steps in planning and executing phase I clinical trials. I will be able to incorporate all of this knowledge in the work at my home institution, Institute of Oncology Ljubljana. Most importantly, I have made new acquaintances at KSSG, especially dr Markus Joerger to whom I am thankful for mentorship during the time and willingness for future cooperation on different projects.

Ljubljana 16th of November

Rok Devjak *Markus Joerger*



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